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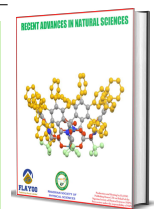

The impact of early detection and intervention on congenital heart defects in infants and children

R. T. Akah*, J. E. Enoh, B. Nkeh-Chungag

Cardio-Metabolic Health Research Group Department of Biological and Environmental Sciences, Faculty of Natural Sciences, Walter Sisulu University (WSU), Nelson Mandela Drive, Private Bag X1, MTHATHA 5117 Eastern Cape, South Africa

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ABSTRACT

Congenital heart disease (CHD) is the leading cause of mortality among congenital disabilities, affecting approximately 1% of live births. This review analyzes the critical role of early detection and intervention strategies in optimizing care for pediatric patients with CHD, utilizing a comprehensive literature search across scientific databases such as Google Scholar, PubMed, Web of Science, Springer Link, and Science Direct for articles published between 2014 and 2024. A total of 10 studies were included, representing diverse populations and healthcare systems, which provided a global perspective on CHD prevalence and diagnosis in infants and children. These studies, comprising case-control studies from Mount Sinai Medical Center, cohort studies from regions such as Denmark, Paris, Saudi Arabia, and Australia, and cross-sectional studies from China and France/Belgium, highlight the clinical challenges associated with CHD and the long-term developmental and psycho-social implications for affected children. The findings underscore the necessity of continued efforts in maternal health, early screening, and holistic care approaches to improve outcomes for children with CHD worldwide. Ultimately, the review emphasizes that early detection is crucial for enhancing survival rates and quality of life and advocates for integrating medical and psycho-social support to address the multifaceted needs of these children.

1. INTRODUCTION

Congenital heart defects (CHD) are birth defect that affects the structure of the heart or blood vessels. These structural abnormalities, such as a small hole in the heart (mild) to missing parts of the heart (severe), present at birth, afflicting about 0.8% to 1.2% of live births worldwide [1, 2]. Although advances in cardiovascular medicine and surgery over the past decades have decreased mortality drastically and enabled most patients to reach adulthood, CHD remains the leading cause of mortality from birth defects and imposes a significant burden on global health. The incidence of CHD varies by geography, ethnicity, and maternal factors [2, 3]. In the United States, recent estimates suggest that CHDs affect about 1% of live births annually, with certain subtypes of CHD being more prevalent in specific populations [4, 5]. Moderate to severe forms of CHD may be observed more

*Corresponding author Tel. No: +27-687-581-635.
e-mail: rakah@wsu.ac.za (R. T. Akah)

frequently in infants of mothers with diabetes mellitus or those exposed to certain teratogens during pregnancy. Data on CHD in low to middle-income countries (LMICS), especially Africa, are limited [4, 6]. Africa has the lowest reported birth prevalence of CHD at 1.9 per 1000 live births, with the prevalence in South Africa estimated to be 0.6-0.8 per 1000 live births, likely underrepresented compared to many patients with CHD in Africa missed [6].

The etiology of CHD remains largely unknown, with only about 15% of cases linked to identifiable factors. Well-recognized chromosomal aneuploidies cause malformation syndromes that comprise 8% to 10% of CHD, like Down syndrome, trisomy 13, trisomy 18, Down syndrome, Turner syndrome, and DiGeorge syndrome [7, 8]. Congenital heart defects (CHD) is influenced by a broad range of risk factors relating to the mother, foetus, and newborn, including the accessibility of primary care, the precision of neonatal assessments, frequencies of prenatal diagnoses, and decisions regarding pregnancy terminations with about 2% of all cases of CHD attributed to known environmental factors [9]. These factors exhibit geographical variations that contribute to the overall birth prevalence of CHD. There are also differences in CHD presentation between men and women [10]. In the latter, the prevalence of atrial septal defect type 2, persistent ductus arteriosus (PDA), and atrial ventricular septal defect is higher. In contrast, outflow tract defects such as transposition of the great arteries, aortic valve stenosis, coarctation, and tetralogy of Fallot are more frequent in men. Infants with CHD often face developmental disabilities, with the likelihood and severity increasing with the complexity of the defect; more than 80% of infants with mild CHD do not have developmental disabilities, compared to over half of those with critical CHD. Research indicates that children with symptomatic CHD at birth are at a heightened risk of adverse neurodevelopmental outcomes by age eight [11], especially those born with both cyanosis and heart failure. Many infants with CHD also experience growth failure in the initial months due to increased energy expenditure, poor feeding, fluid restrictions, or diuretic use, and there is no consensus on standardized nutritional management for these patients. Fetal echocardiograms can detect some heart defects during pregnancy [10, 11], while others may not be identified until birth or later in life; if a healthcare provider suspects a defect, several tests, including echocardiograms, may be conducted to confirm the diagnosis. Other heart defects aren't detected until birth or later in life, during childhood or adulthood [8, 11].

After birth, newborn screening for critical heart defects can help identify babies whose heart defects were not detected during pregnancy. Newborn screening for essential defects of the heart involves a simple bedside pulse oximetry test [12]. This test estimates the amount of oxygen in a baby's blood. Low oxygen levels in the blood can indicate a critical heart defect. Screening newborns for heart defects enables them to be treated early and may prevent other health problems or early death. The absence of CHD screening using pulse oximetry and early interventions during the neonatal stage also contributes to premature fatalities [13]. Alongside prevalence and mortality rates, assessing the incidences of CHD-related morbidity, such as developmental impairments and the quality of life, is crucial in determining the impact of CHD.

Early diagnosis and prevention of cardiovascular disease such CHD remains a critical focus, especially for high-risk populations, and is crucial for effective management and improvement of patient (Infant) outcome [14]. Advancements in diagnostic techniques for congenital heart defects (CHDs) have significantly improved prenatal and postnatal evaluation, enhancing clinical outcomes [15]. Fetal echocardiography has revolutionized prenatal diagnosis by facilitating early interventions and improving care planning, while advancements in transthoracic and transesophageal echocardiography have enhanced imaging quality, including the introduction of techniques like tissue Doppler imaging and three-dimensional [16] echocardiography for more accurate assessments. Cardiovascular magnetic resonance imaging (CMR) offers detailed anatomical and functional insights without the limitations of radiation exposure and is supported by techniques such as flow quantification and Gadolinium-enhanced angiography. Other imaging modalities like computed tomography and positron emission tomography also play essential roles in assessing cardiac structures and pathological processes [16, 17]. Biomarkers, including BNP and troponins, are increasingly recognized for their diagnostic and prognostic value in CHDs, aiding in the management of patients. Additionally, innovative e-health solutions and new monitoring devices are emerging, improving patient management through telehealth and real-time data collection, thereby enhancing the detection of complications and overall care for those with congenital heart disease [18, 19].

In the treatment of congenital heart disease (CHD), significant advancements have been made in both medication and catheter-based procedures. Historically, medical therapies were often based on pathophysiological assumptions, such as the 2010 European Society of Cardiology guideline recommending digoxin for systemic right ventricular failure without strong clinical evidence [19, 20]. However, recent research has focused on pharmaceutical interventions, revealing the benefits of β-blockers, angiotensin-converting enzyme inhibitors, and specific treatments for pulmonary arterial hypertension (PAH), such as bosentan and sildenafil, which have notably improved patient prognoses. Furthermore, catheter-based interventions have increasingly replaced conventional surgical approaches, with techniques like percutaneous closure of atrial septal defects and patent ductus arteriosus becoming standard practice due to advancements in device technology. While significant progress has been achieved, conducting adequately funded clinical trials remains essential to establish more evidence-based practices in CHD treatment, especially as administrative burdens and costs pose challenges to ongoing research and development. Early detection and timely intervention are crucial in managing CHD and improving quality of life outcomes.

This review seeks to provide a comprehensive analysis of the role of early detection and intervention strategies in optimizing care for pediatric patients with CHD.

1.1. OBJECTIVES

1. To assess the effectiveness of early screening programs in identifying congenital heart defects in infants and children.
2. To evaluate the impact of timely intervention and treatment modalities on the outcomes and prognosis of pediatric pa-

tients with CHDs.

3. To identify challenges and barriers to early detection and intervention for congenital heart defects in pediatric populations.

2. MATERIAL AND METHODS

The protocol was registered with PROSPERO (registration no. CRD42024558077). The review included full English articles reporting on the impact of early detection and intervention on congenital heart defects in infants and children. The review also included studies published from 2014 to 2024 with cross-sectional, cohort, and case-control study design. Those excluded were non-peer-reviewed articles, grey literature, CHD in adults, and non-English language publications.

2.1. LITERATURE SEARCH AND STUDY SELECTION

Electronic databases (PubMed, Springer Link, Web of Science, Google Scholar, and Science Direct) will be systematically searched for relevant studies published between [2014] and [2024]. Search terms will include variations of "congenital heart defects", "early detection", "intervention", "infants", "children", and "quality of life."Data Extraction: Relevant data on study characteristics, participant demographics, intervention methods, outcomes, and quality of life assessments will be extracted and synthesized.

2.2. QUALITY ASSESSMENT

Included studies will be evaluated for methodological quality and the risk of bias using appropriate tools (Newcastle-Ottawa Scale for observational studies). By employing the Newcastle-Ottawa Scale, this review provides a structured and standardized approach to assess the quality of the studies evaluated, ultimately enhancing the reliability and validity of the findings related to congenital heart disease outcomes.

2.3. DATA SYNTHESIS

Findings will be analyzed descriptively and, if feasible, through meta-analysis to assess the overall impact of early detection and intervention on CHDs in infants and children. Two reviewers reviewed the titles and abstracts independently to determine their relevance. The reviewers also conducted the extraction independently to ensure accuracy and reliability.

3. RESULTS

A total of the 10 studies conducted across different countries, focusing on congenital heart disease (CHD) and its associated outcomes in infants and children published between 2014 and 2024, are shown in Table 1. It illustrates the evolving research landscape that emphasizes not only the immediate clinical challenges of CHD but also the long-term developmental and psychosocial outcomes for affected children. The early detection plays a crucial role in improving survival rates, quality of life, and long-term outcomes for affected children. It enables timely interventions, minimizes complications, and supports ongoing care, thus enhancing the overall management of CHD. The findings call for continued efforts in maternal health education, early screening, support programs for families, and holistic care approaches to improve the lives of children with CHD worldwide.

Studies in the USA, Canada, Denmark, China, France, Belgium, Saudi Arabia, Latin America, and Australia suggest a broad international interest in the epidemiology of congenital heart disease. The design consists of case-control studies conducted at Mount Sinai Medical Center, which compare congenital heart disease (CHD) cases with controls. Cohort studies from Denmark, Paris, Saudi Arabia, and Australia aim to track specific populations over time to observe outcomes related to CHD, and cross-sectional studies from China and France/Belgium provided a snapshot of prevalence and associations at a particular point in time.

The Regional trends in congenital heart disease (CHD) management reveal distinct focuses: North America (U.S. and Canada) emphasizes effective management strategies and maternal health; Europe (Denmark, France, Belgium) prioritizes psychosocial care and the relationships between specific defect types and outcomes; Asia (China) promotes collaborative care and early screening for congenital and prematurity-related issues; the Middle East (Saudi Arabia) highlights prevalent CHD types, reflecting regional variances; while Latin America focuses on genetic and chromosomal factors that contribute to mortality, showcasing the unique healthcare dynamics within the region.

Newborn screening outcomes highlight the importance of early diagnosis, as seen in a nationwide study in China that supports the implementation of CHD screening programs. Additionally, a cohort study in Denmark identified specific CHD subtypes associated with smaller head circumferences, and research from Australia underscored the significance of monitoring growth patterns in infants with CHD for better cognitive and motor outcomes. Intervention effectiveness is demonstrated through findings from Mount Sinai Medical Center, USA, where effective management strategies reduced the prevalence of comorbidities. A study in Quebec, Canada, linked maternal preeclampsia to noncritical heart defects, emphasizing the role of maternal health. In China, preterm and low birth weight infants were found to have higher prevalence rates among critical CHD cases, pointing to the need for integrated care strategies. Moreover, research in France and Belgium highlighted the necessity of psychosocial support for affected families. At the same time, a study in Saudi Arabia indicated the predominance of specific CHD types, suggesting targeted interventions. Lastly, a retrospective study in Latin America and the Caribbean revealed that chromosomal anomalies contribute to excess mortality in CHD, informing future intervention efforts.

4. DISCUSSION

This systematic review seeks to assess the effectiveness of early screening programs in identifying congenital heart defects in infants and children. Early screening programs for congenital heart disease can significantly improve clinical outcomes by facilitating early interventions, reducing mortality and morbidity rates, enhancing quality of life, and enabling effective long-term monitoring and support [20, 21].

Maternal health factors significantly influence the development of congenital heart disease (CHD) in infants, with various conditions adversely affecting fetal heart development. Ma-

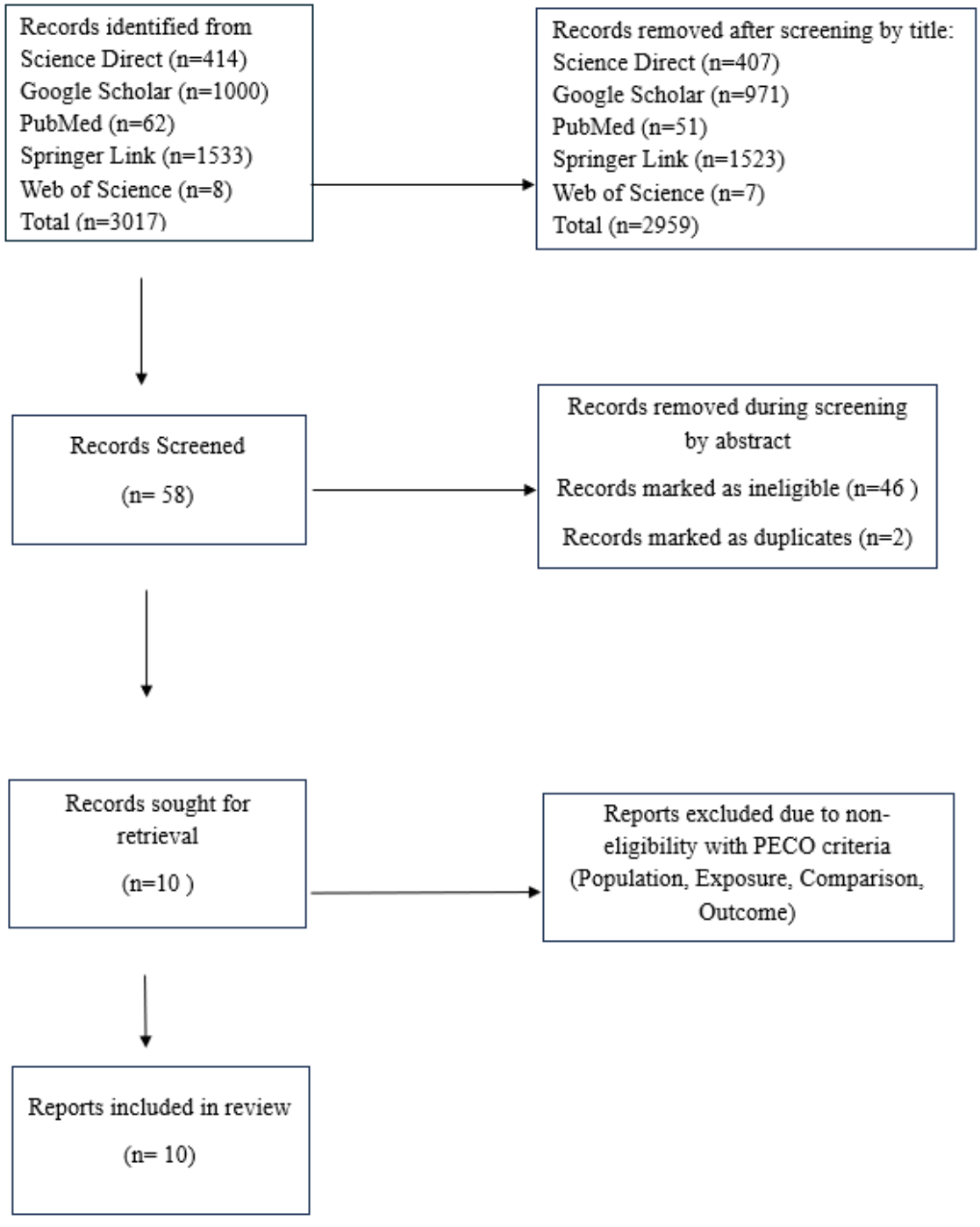

Figure 1. PRISMA flow diagram.

ternal health issues include preeclampsia, which is linked to an increased risk of noncritical heart defects, mainly when poorly managed due to insufficient prenatal care. Pregestational and gestational diabetes elevates the likelihood of CHD in infants, primarily through metabolic changes. Advanced maternal age is also a risk factor, as women aged 35 and older face higher rates of chromosomal abnormalities and complications during pregnancy. Additionally, maternal obesity correlates with a greater incidence of congenital defects, largely due to associated health issues such as gestational diabetes and hypertension. Other health conditions, including autoimmune disorders and infections during pregnancy, further contribute to the risk of CHD. These findings emphasize the critical need for comprehensive maternal healthcare and proactive management of maternal health conditions to improve outcomes for both mothers and their children and reduce the incidence of congenital heart defects. Early screening can be further inferred from the studies that linked maternal health factors to CHD, indicating that better maternal screening may allow for proactive monitoring and management of high-risk pregnancies [13, 22, 23].

Table 1. Characteristics of included studies on detection and intervention on congenital heart defects in infants and children.

Country	Study design	Sample size	Population	Outcome	Reference
Mount Sinai Medical Center, New York, NY, USA	Case-control study design	live births with CHD diagnosis (case= 97,154) and live births without CHD diagnosis (control= 12,078,482)	Newborns	There was a significant decrease in the prevalence of syndromic malformations and multiple organ-system congenital abnormality (CA) in the CHD population, indicating effective management leading to fewer comorbidities.	Egbe *et al.* 2014 [1]
The entire province of Quebec, Canada	population-based study	1 942 072 infants delivered at 20 weeks of gestation or more in this study, including 17 296 with heart defects. The sample included 50 840 multiple births	Infants	Preeclampsia was significantly associated with noncritical heart defects in offspring, highlighting the impact of maternal health on fetal heart development.	Auger *et al.* [22]
Denmark	Prospective Cohort from 1997 to 2011	924 422 infants of which 5519 were registered with CHD	Newborns	Specific subtypes of CHD were linked with smaller head circumference (HC), particularly in infants with transposition of the great arteries, indicating that certain defects may lead to malformation.	Matthiesen *et al.* [24]
China	cross-sectional observational study between August 1, 2011, and November 30, 2012	122 765 deliveries were eligible for our CHD prevalence analysis	Newborn	The study found that preterm infants and low birth weight infants were more prevalent among those with critical CHD cases. This emphasizes the potential need for integrated care strategies that concurrently address prematurity and congenital conditions.	Zhao *et al.* [25]
France and Belgium	comparative cross-sectional study between April 2009 and October 2011 (18 months)	282 CHD patients and 180 controls	children	The study contributes crucial insights into health-related quality of life for children with congenital heart disease, emphasizing the necessity for both medical and psychosocial support to enhance life quality for affected families	Amedro *et al.* [11]
Shanghai China	an observational study from January 1, 2017, to December 31, 2021	801,831	Newborn	The study provided strong evidence for the nationwide implementation of CHD screening programs, promoting early diagnosis and intervention in China.	Ma *et al.* [21]
Paris, France	prospective population-based cohort study	2172	Newborns	Preterm birth is associated with an approximately four-fold higher risk of infant mortality for newborns with CHD	Laas *et al.* [26]
Saudi Arabia	Prospective cohort study	264	children	Septal defects and right-sided pathologies are the dominant forms of congenital heart diseases, with atrioventricular septal defect and perimembranous ventricular septal defect representing the most common pathologies	Alkhushi [27]
Latin America and Caribbean, French Guiana	retrospective observational study, 1 year (January 2012–December 2016	33,796	infants	A potential determinant of the recognized excess mortality risk might be the presence of chromosomal or genetic anomalies in about a fifth of all CHD thus helping better to understand the CHD burden in this part of South America and providing future keys towards reducing CHD-related infant mortality	Lucron *et al.* [28]
Australia	retrospective cohort study between Jan 2016 to Dec 2020	184	newborns	The study offers valuable insights into the growth patterns and neurodevelopmental outcomes of infants with congenital heart diseases, especially emphasizing the significance of adequate postnatal growth and its impact on cognitive and motor skills. This information is critical for guiding clinical practice and shaping further research in the management of children with CHD	Trivedi *et al.* [7]

The prospective cohort study in Paris emphasizes that early detection of CHD through screening could lead to enhanced prenatal care and interventions in preventing preterm deliveries or better managing these infants post-delivery, effectively reducing mortality rates [26]. Additionally, the study from Denmark noted that certain CHD subtypes are associated with specific growth patterns, suggesting that these associations can lead to tailored interventions, such as nutritional support for infants with specific heart conditions [24]. The study in France and Belgium underscored that screening offers the opportunity for immediate medical intervention and also for implementing comprehensive care strategies that consider both physical health and quality of life issues for affected children [11]. Thus, early identification allows families to prepare and seek appropriate social support, which is crucial for long-term developmental outcomes [23, 29, 30]. Furthermore, the retrospective cohort study from Australia suggested that screening can facilitate this longitudinal monitoring and intervention, ensuring that follow-up measures are in place to support healthy growth and development, which are vital for these children's overall well-being [7]. Lucron and collaborators identified that genetic factors through screening can lead to personalized care pathways that address specific risks associated with identified anomalies [28]. As highlighted in the studies, the integration of medical and psychosocial care approaches following early detection is crucial for optimizing outcomes and addressing the complex needs of children with CHD. The positive implications of these findings advocate for the broader implementation of newborn screening programs on a global scale to ensure that infants with CHD receive the necessary care from birth, ultimately improving survival and quality of life [5, 31].

In the process of assessing the impact of timely intervention and treatment modalities on the outcomes and prognosis of pediatric patients with CHDs, Egbe *et al.* [1] indicate that timely interventions can reduce the prevalence of syndromic malformations and multiple organ-system congenital abnormalities thus, early medical attention and possibly screening can mitigate the severity and complexity of coexisting congenital conditions [1, 32]. Moreover, research from Denmark [24] highlights that specific CHD subtypes, especially transposition of the great arteries, can be associated with smaller head circumference, indicating a need for interventions targeted at growth and development in infants with specific heart conditions hence, timely interventions may help to optimize developmental outcomes [5, 17, 19]. Amedro *et al.* [11] shed light on the quality of life for children with CHD, suggesting that timely surgical, medical, and psychosocial interventions like counseling, support groups, and recreational therapy, to name these, are necessary for optimizing life quality and the importance of holistic approaches in managing CHD, which could lead to better long-term outcomes [3, 11, 20]. The evidence from these studies collectively underscores the critical nature of timely interventions and treatments for congenital heart disease. A proactive approach involving early detection, managing maternal health, integrating healthcare strategies, and considering psychosocial aspects can significantly improve outcomes for optimal development and quality of life [33, 34].

Identifying challenges and barriers to early detection and intervention of congenital heart disease (CHD) from the studies reveals a complex set of issues at various levels related to maternal health, monitoring practices, and healthcare infrastructure. The Quebec study identified a significant association between preeclampsia and both noncritical and critical heart defects, indicating that maternal conditions can hinder early identification of CHD if not properly managed [17, 22]. Similarly, research from Denmark linked specific CHD subtypes, notably transposition of the great arteries, to smaller head circumferences, pointing out gaps in routine growth monitoring for high-risk populations [24, 35]. The study from China noted that preterm and low birth weight infants had higher rates of critical CHD, emphasizing the need for tailored screening programs for these vulnerable groups [9, 25].

Meanwhile, the Shanghai study supported the implementation of a nationwide newborn screening program for CHD, yet challenges such as inadequate healthcare infrastructure and the need for trained personnel could impact its effectiveness [21, 36]. Research from France and Belgium stressed the importance of raising awareness among healthcare providers and families about the critical need for early screening, as a lack of understanding can lead to missed opportunities [10, 11]. Additionally, findings in Latin America revealed that many CHD cases involve genetic anomalies, and the absence of routine genetic screening can hinder early diagnosis [28]. Finally, the Australian study underscored the importance of effective follow-up for ensuring adequate postnatal growth, essential for cognitive and motor outcomes, highlighting challenges when families lack access to ongoing monitoring and support [7, 35].

5. CONCLUSION

This review, with diverse studies, demonstrates and collectively reinforces the varied nature of congenital heart disease (CHD), revealing critical insights into its prevalence, associated risk factors, and the significance of comprehensive care strategies. They emphasized the crucial impact of maternal health on fetal outcomes, stressed the need for early detection through effective screening programs, and highlighted the importance of integrated care for both congenital disabilities and associated issues like preterm birth and low birth weight. Moreover, the results emphasized the psychosocial aspect of care, advocating for continuous support for affected families. These studies advocate for a holistic approach to CHD management to improve immediate health outcomes and the long-term quality of life for individuals with this condition.

Despite the valuable information acquired from these studies on congenital heart disease (CHD), several constraints should be considered. The absence of African-based studies on congenital heart disease (CHD) significantly limits the generalizability of findings from research conducted in North America, Europe, and Asia. This gap hinders our understanding of genetic, environmental, and socio-economic factors influencing CHD prevalence and management within diverse African populations. Differences in healthcare systems, socio-economic challenges, and cultural beliefs further complicate the application of international findings to the African context, making it difficult to assess the effectiveness of interventions. Additionally, the variability in disease presentation due to local conditions may lead to misdiagnoses or inappropriate management strategies. To improve the relevance and accuracy of CHD research and interventions, it is crucial to include African populations in future studies, promoting culturally sensitive healthcare approaches and ultimately enhancing health equity on a global scale. The studies used varied designs, sample sizes, and population demographics, which may lead to inconsistencies in findings and limit the generalizability of results across different settings. Some studies, like retrospective ones, introduce biases based on how data was collected or interpreted. Additionally, some studies concentrated solely on specific subtypes of CHD, potentially overlooking the broader spectrum of congenital heart conditions. The reliance on current health records and self-reported data in some analyses may also result in misclassification or incomplete information, potentially affecting the outcomes. Finally, differences in cultural and healthcare resource disparities among the countries studied could influence the prevalence and management of CHD, thus affecting the applicability of findings to diverse populations. These limitations demonstrate the need for further research using consistent methods to understand the complex nature of CHD better globally.

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DATA AVAILABILITY

We do not have any research data outside the submitted manuscript file.

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